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University of Oklahoma HSC

Modeling Risk Reduction Interventions for Patients with Type 2 Diabetes Mellitus

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Value to the Customers (AHRQ, researchers, and clinicians)

Value: Documentation of complexity

Example: Standard quality indicators fail to account for complexity.

Value: Demonstration of benefit of Archimedes model

Example: Could be used at the point of care to guide decision-making.

Value: Demonstration of diminishing returns principle

Example: Three interventions are nearly as good as eight if well-chosen.

Disclosure Information

Name/Date of Meeting Here

Name of Speaker Here

Disclosure of Relevant Financial Relationships

I have the following financial relationships to disclose:

Grant/Research support from: AHRQ, NHLBI

I have no other financial relationships to disclose.

Disclosure of Off-Label and/or investigative Uses

I will not discuss off label use and/or investigational use in my presentation.

Complex Patients Require Complex Treatment Decisions

- Multiple Possible Adverse Outcomes
  - Which are most likely?
  - Which are most important?
- Multiple possible interventions
  - Which should be recommended first, second, third?
- Diminishing Returns
  - How many interventions are enough?

Patients with Type 2 Diabetes are Complex

Other health conditions are often present

- Hypertension
- High LDL; low HDL; high triglycerides
- Obesity and/or Inactivity
- Macrovascular disease (CAD, PAD, CVD)
- Microvascular disease (renal, eye)
- Peripheral and/or autonomic neuropathy
- CHF

Multiple guidelines often apply

Modeling Outcomes in Diabetes

Cardiff Diabetes Model (Discrete Events)

UKPDS Outcomes Model (Discrete Events)

UKPDS Risk Engine (Regression)

EAGLE (Monte Carlo)

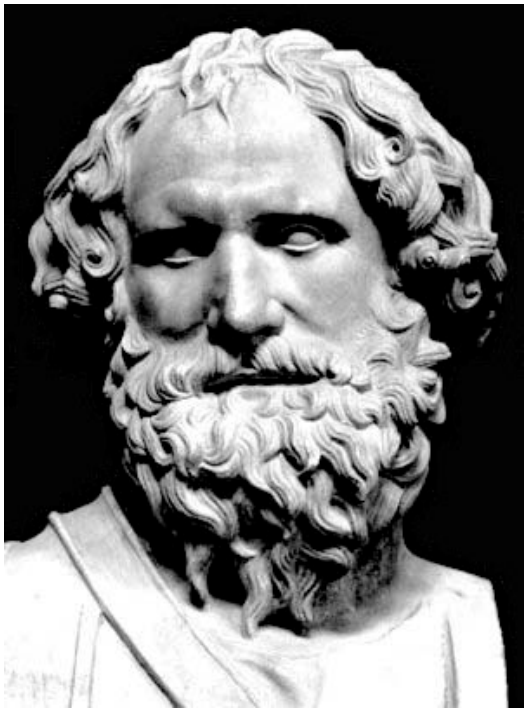
CORE Diabetes Model (Monte Carlo)

Sheffield Diabetes Model (Progression Model)

CDC/RTI Type 2 Diabetes Progression Model

Archimedes (Object-Oriented Modeling)

Archimedes



How it works

- Object oriented programming
- Differential equations to represent biological information
  - Biochemistry, physiology, pathophysiology
  - Signs and symptoms
  - Treatment
  - Behaviors and logistics
  - Treatments
  - Outcomes
  - Costs

Diabetes PhD - a simplified version, is available on a public website through the American Diabetes Association

PHD Validation

Subjected to a series of 74 validation exercises involving 18 clinical trials, 10 of which were not used in the construction of the engine

Correlation between results of PHD simulations and clinical trials overall was astounding (r=0.99)

Correlation between absolute differences in outcomes also amazing (r=0.97)

Predicted lower effectiveness of aspirin in women, increased MI risk in older patients with A1cs <7%

Outline of the Research

Create simulated patient prototypes with varying severities of hypertension, dyslipidemia, glucose control, etc.

Determine their predicted risk of specified outcomes at 10, 20 and 30 years

Determine the size of risk reductions for different interventions, individually and in combination

Patient Prototypes

(Variables and their possible values)

Gender	Male, female
Age	40, 50, 60, 70, 80
Race, ethnicity	WNH, H, B, A, AI
BMI	25, 27, 30, 35
Systolic BP / Diastolic BP	130/80, 140/90, 160/100, 180/110
LDL	70, 100, 130, 160, 190
HDL	30, 40, 50, 60
Triglycerides	100, 150, 300, 500
HbA1c	7, 8, 9, 10, 12
Smoking	Current, Past, Never
Physical activity	Sedentary, Light, Moderate, Vigorous
Conditions, macrovascular	None, MI, CVA, Angina, CABG/Angioplasty/Stent, CHF
Conditions, eye	None, Retinopathy, Blindness from Diabetes, Laser
Conditions, renal	None, Proteinurea, Dialysis or Transplant
Conditions, extremities	None, Foot ulcers, Amputation

Interventions

(Possible interventions with possible levels of impact on intermediate outcomes)

Tobacco use cessation	Yes, no
Physical activity	Sedentary, light, mod., vigorous
Weight reduction	25, 27, 30
BP reduction	130/80, 140/90, 160/100
LDL reduction	70, 100, 130, 160
ACEI/ARB	Yes, no
Beta blocker	Yes, no
Blood glucose control	Yes, no
Low dose aspirin	Yes, no
Annual foot exams	Yes, no
Annual eye exams	Yes, no

Outcomes

Cumulative Risk over 10, 20, and 30 years of:

- MI
- Stroke
- Renal failure
- Retinopathy
- Blindness
- Foot ulcers
- Amputation

Challenges

Variation in calculated risks with same inputs

- Diabetes PHD applies the input values to a hypothetical 1,000 pt cohort and yields a mean
- Some parts of the model are probabilistic
- Estimates are problematic especially for low risk outcomes

Number of possible combinations

- Basic prototypes – 69,120
- Interventions – 109,276
- Total - 7,553,157,120
- It is only feasible to run each prototype once

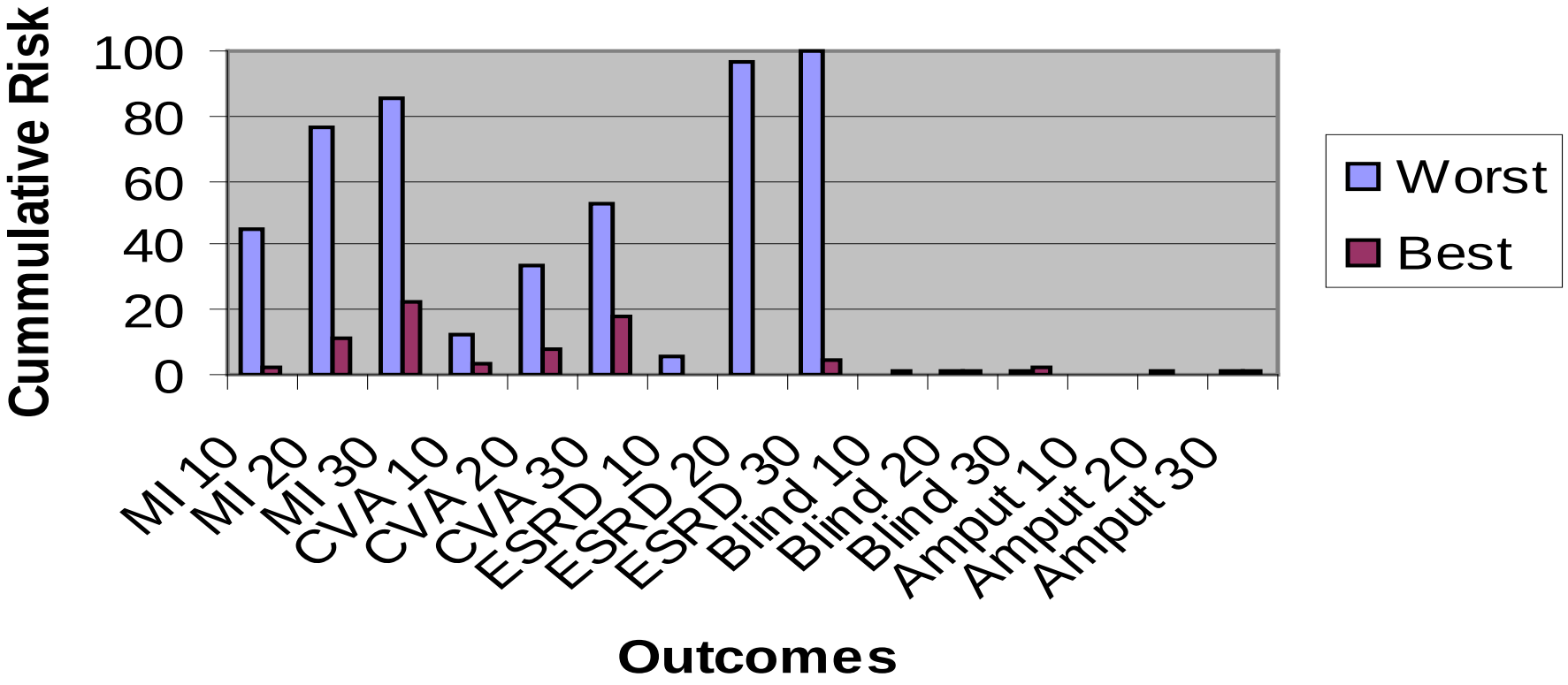
Simulated patients for Demonstration

50 year-old white males with a four year history of Type 2 diabetes

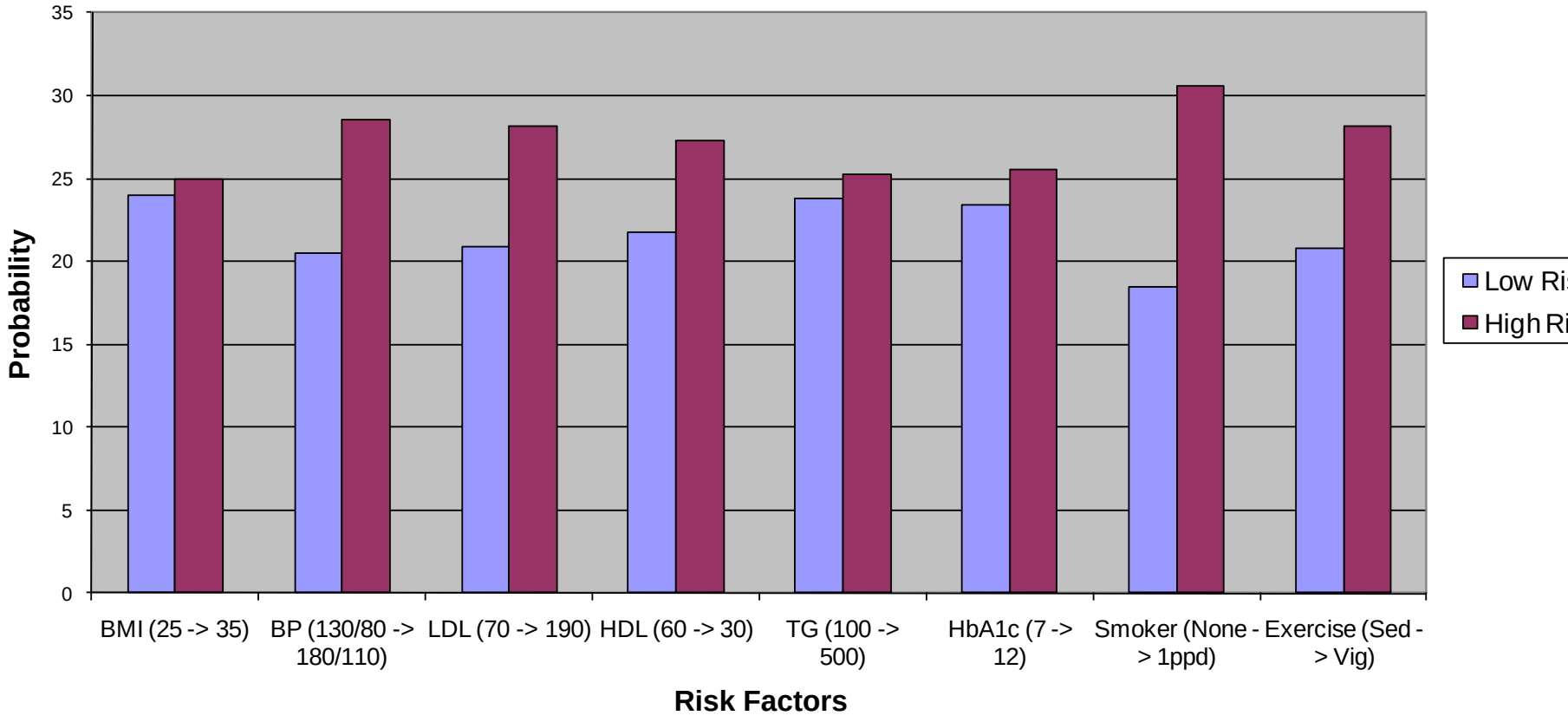
Prototype variable values:

- BP: 130/80, 180/110
- LDL: 70, 190
- HDL: 30, 60
- Triglyceride: 100, 500
- A1c: 7%, 12%
- BMI: 25, 35
- Smoker (16yo), non-smoker, former smoker (just quit)
- Sedentary, vigorous exercise

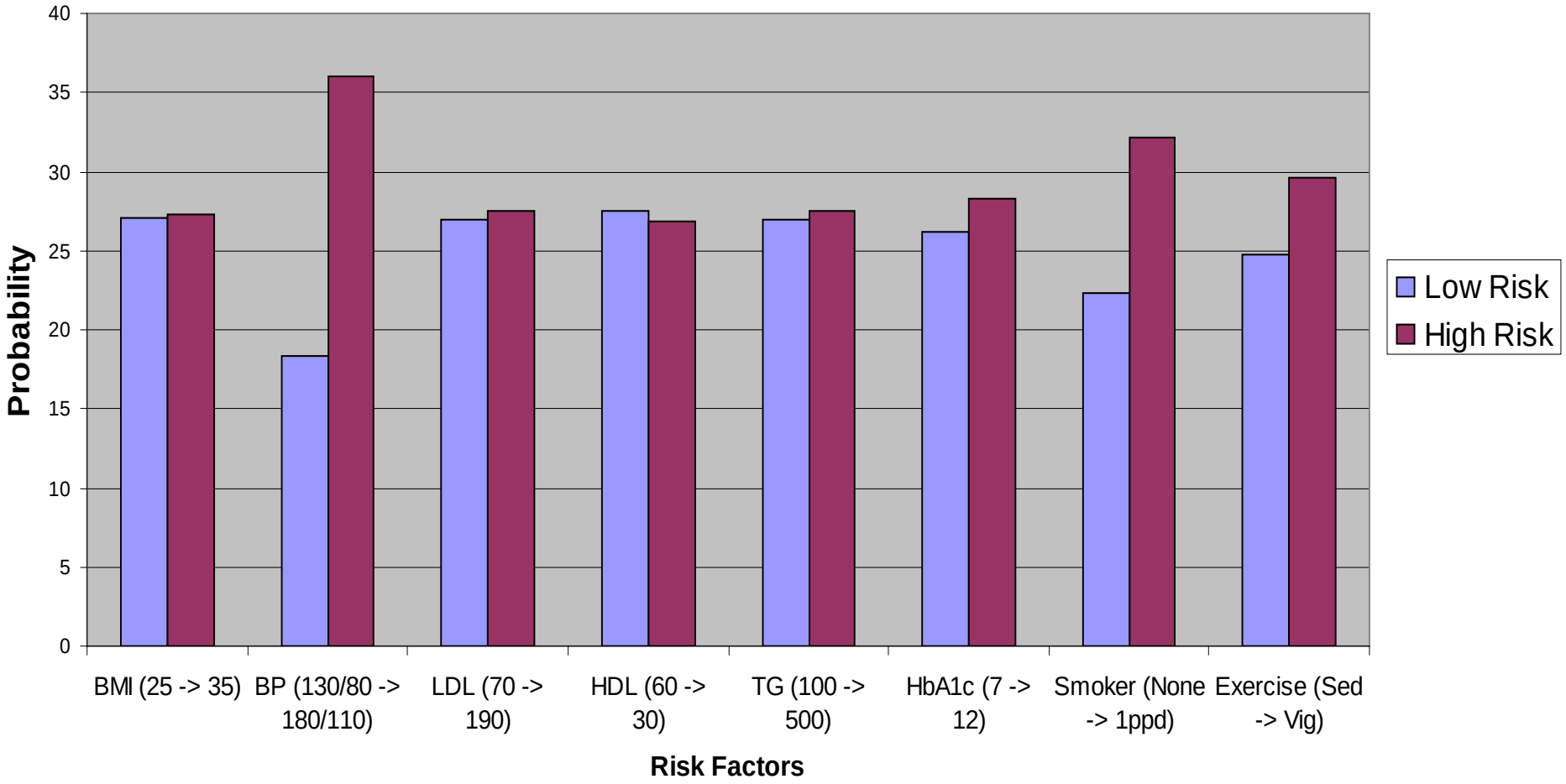
Outcome Probabilities 50 y.o. WM with DM and many vs few other risk factors



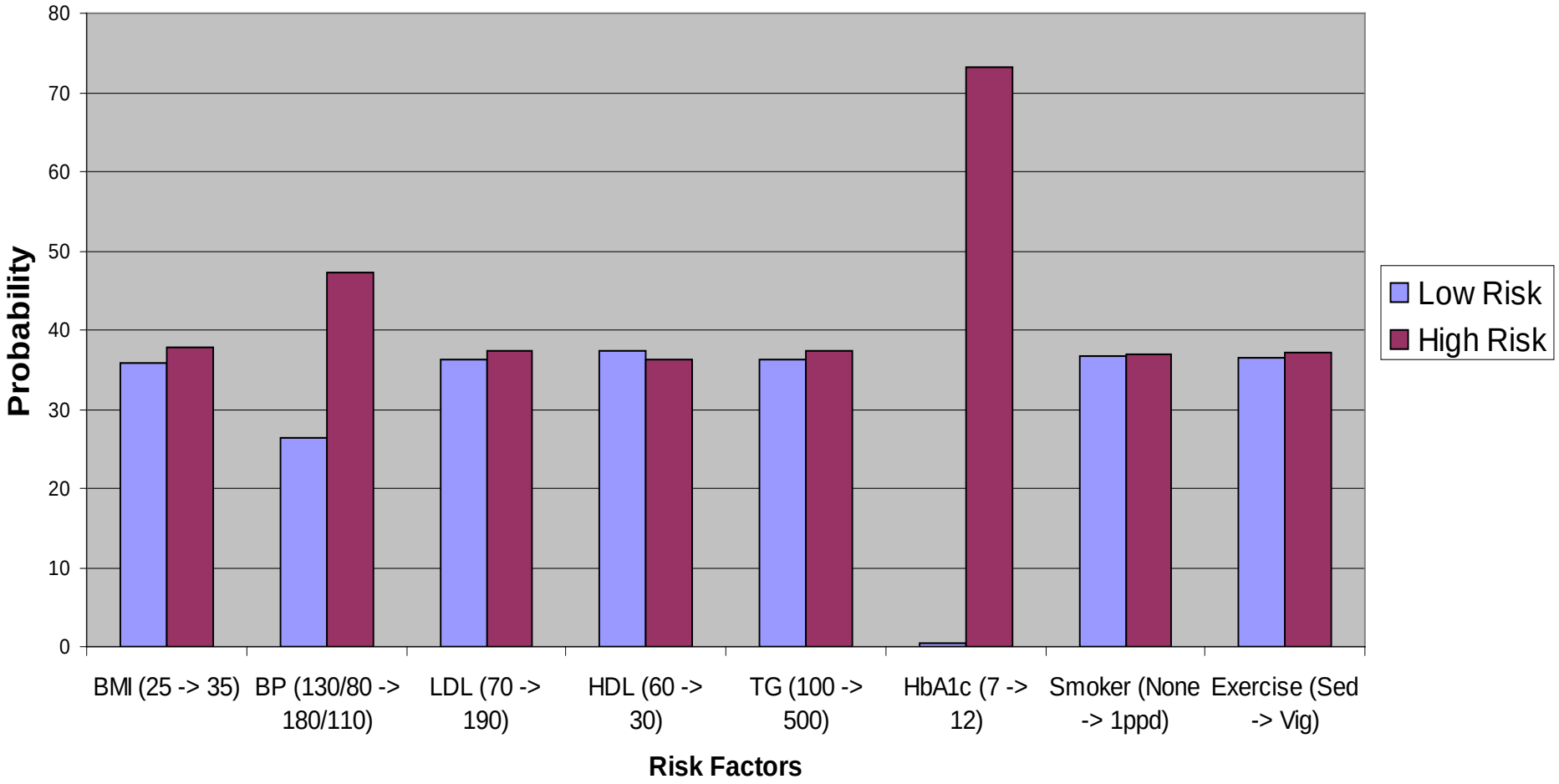
20 Year Risk of Myocardial Infarction



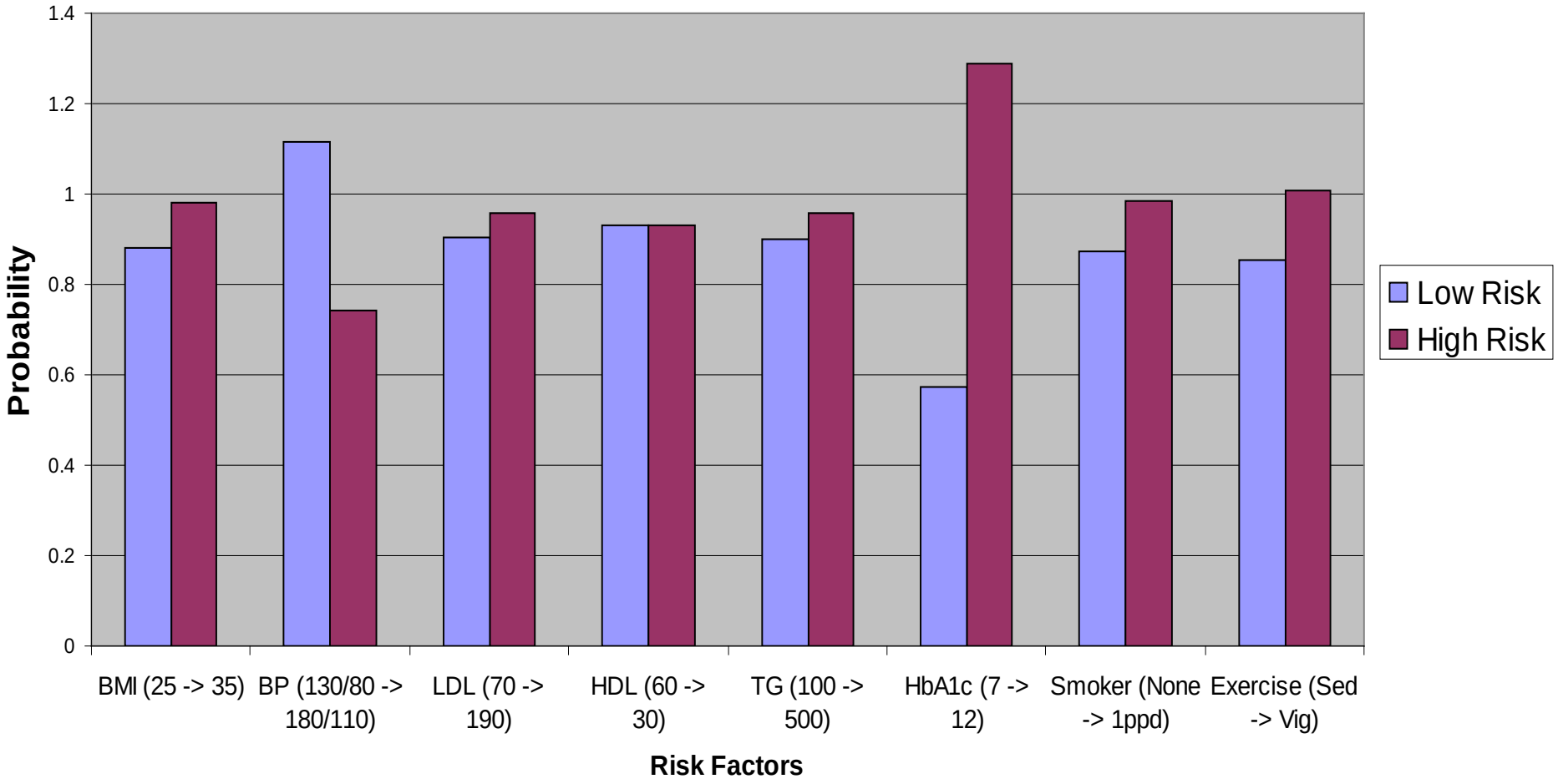
20 Year Risk of Stroke



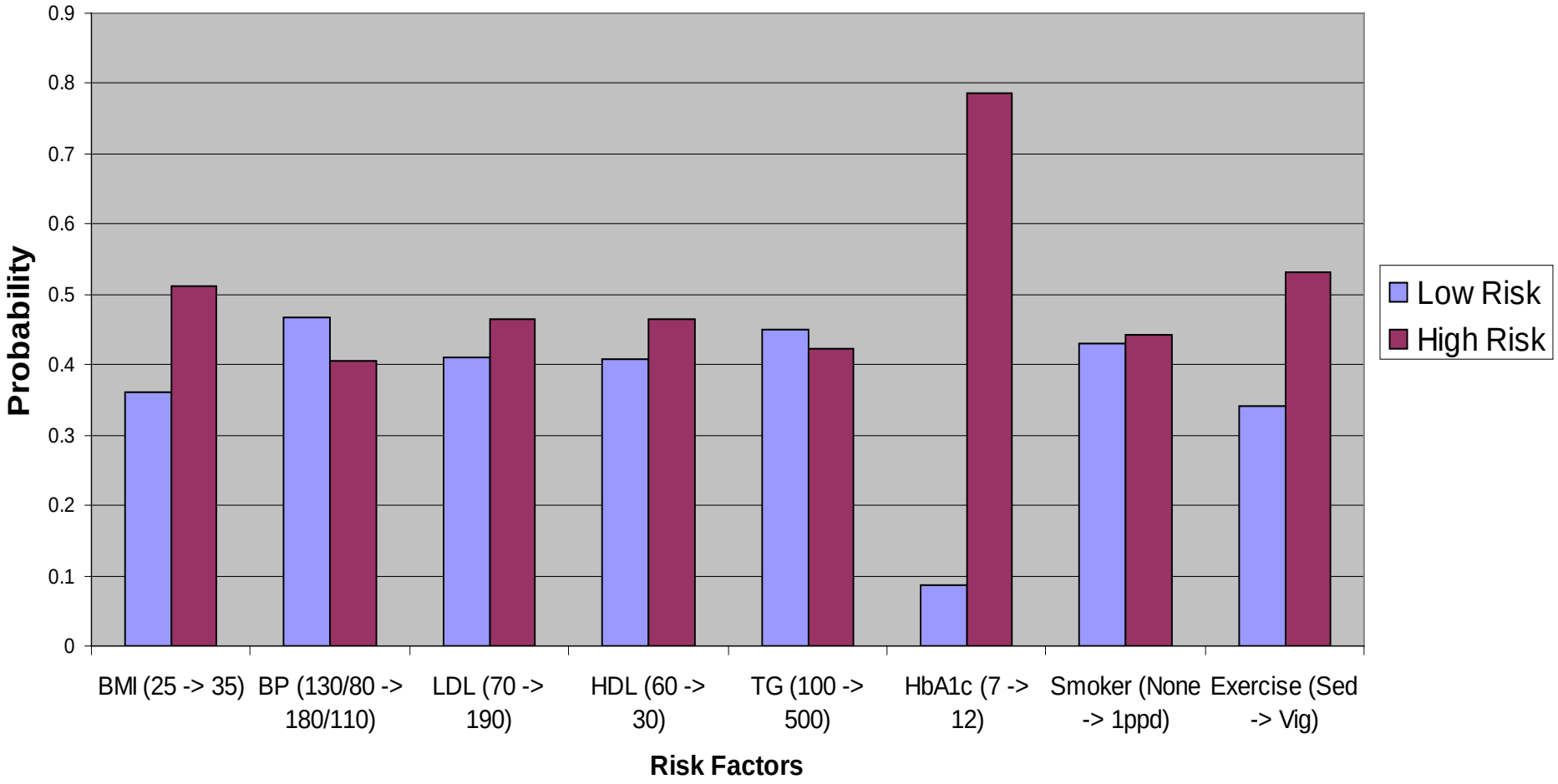
20 Year Risk of Renal Failure



20 Year Risk of Blindness



20 Year Risk of Amputation

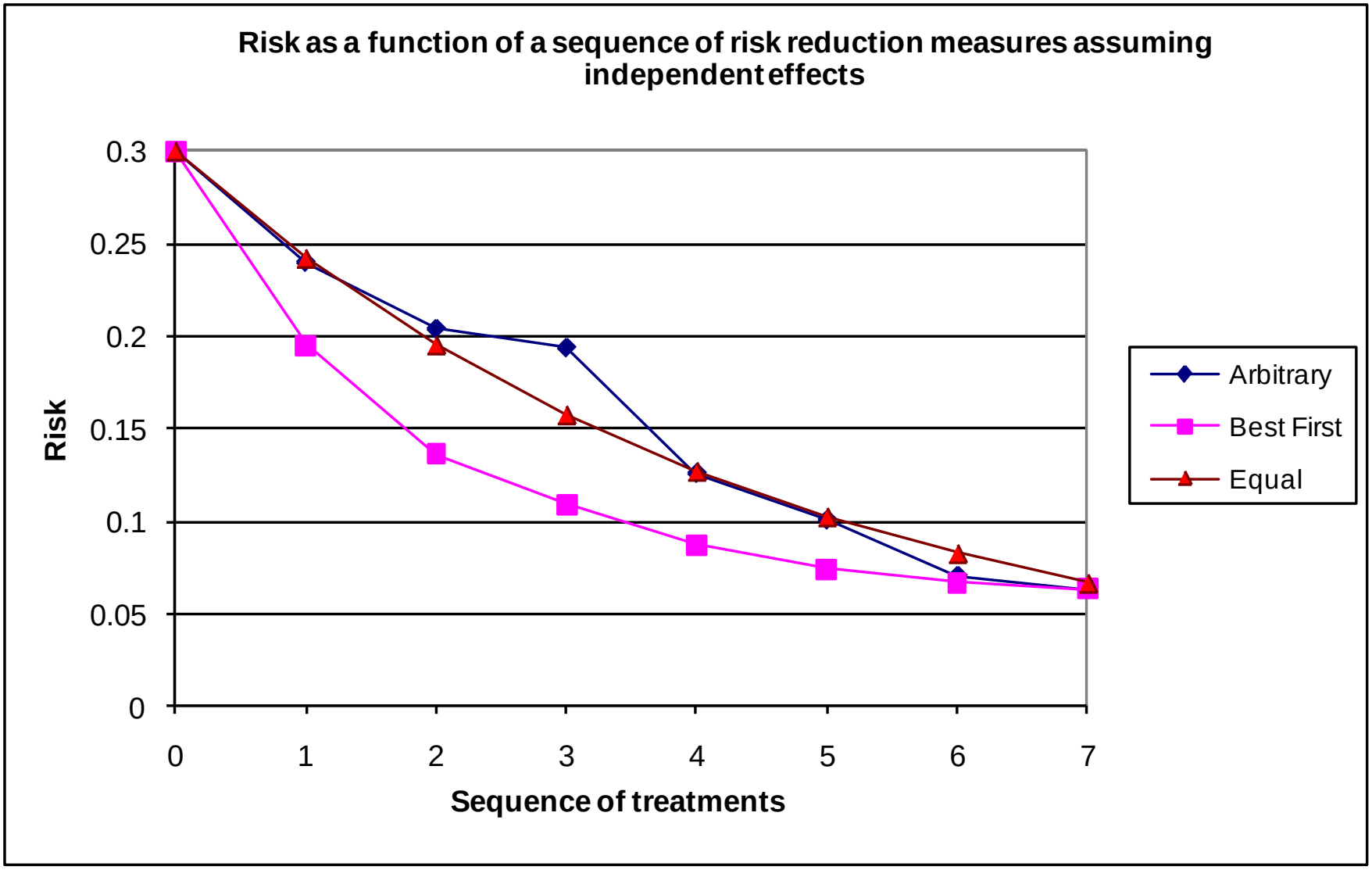


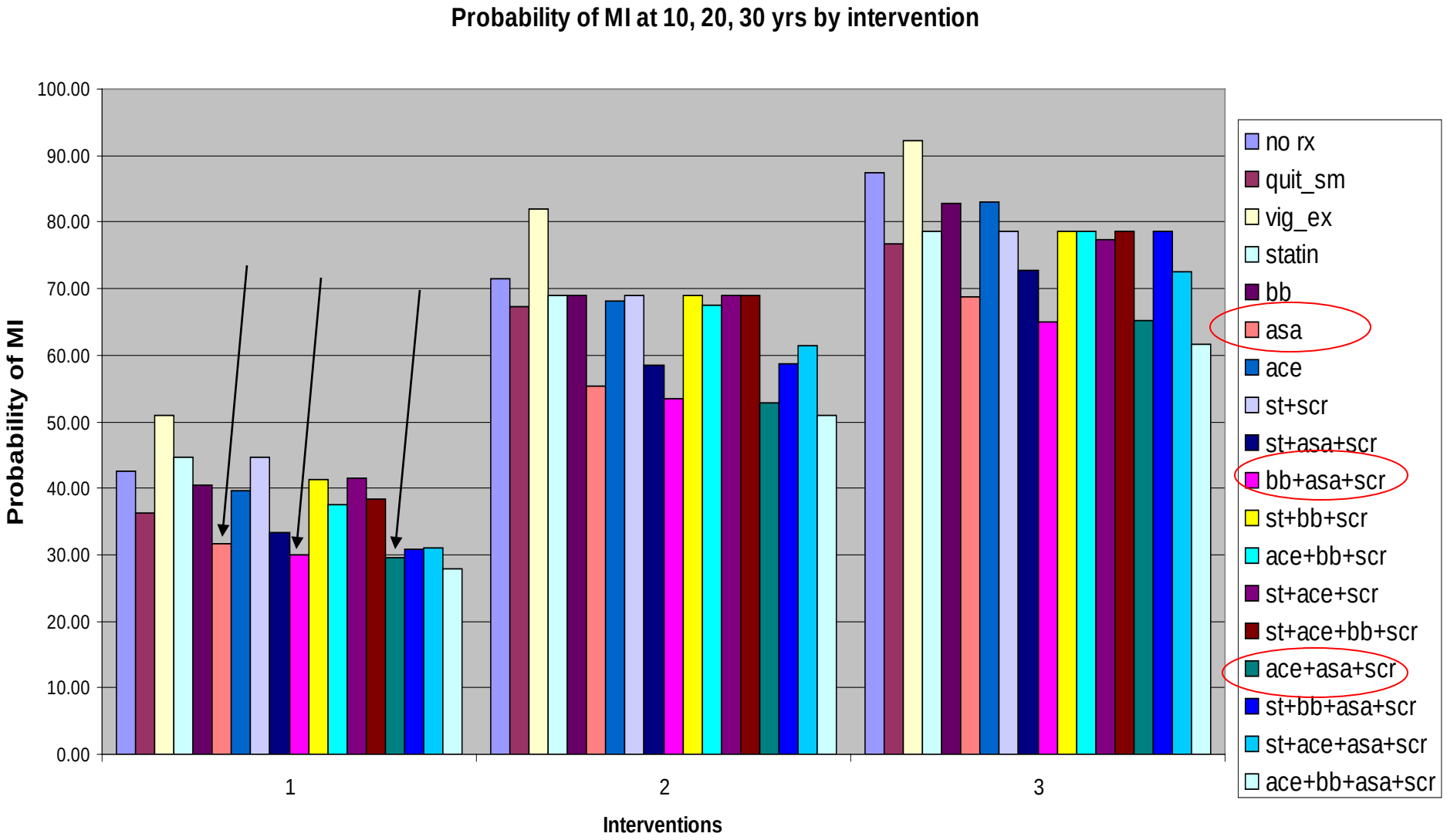
Diminishing Returns

When there are many different ways to reduce the risk of a particular adverse event (e.g. MI), the absolute impact of each successive intervention will be reduced by the impact of prior interventions.

Absolute Risk Reduction = Risk X Relative Risk Reduction

Each intervention reduces risk, so ARR gets smaller if RRR is the same size or smaller.


Risk as a function of a sequence of risk reduction measures assuming independent effects
Risk
0.3
0.25
0.2
0.15
0.1
0.05
0
0
1
2
3
4
5
6
7
Sequence of treatments
Arbitrary
Best First
Equal


Probability of MI at 10, 20, 30 yrs by intervention
Probability of MI
100.00
90.00
80.00
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00
1
2
3
Interventions
no rx
quit_sm
vig_ex
statin
bb
asa
ace
st+scr
st+asa+scr
bb+asa+scr
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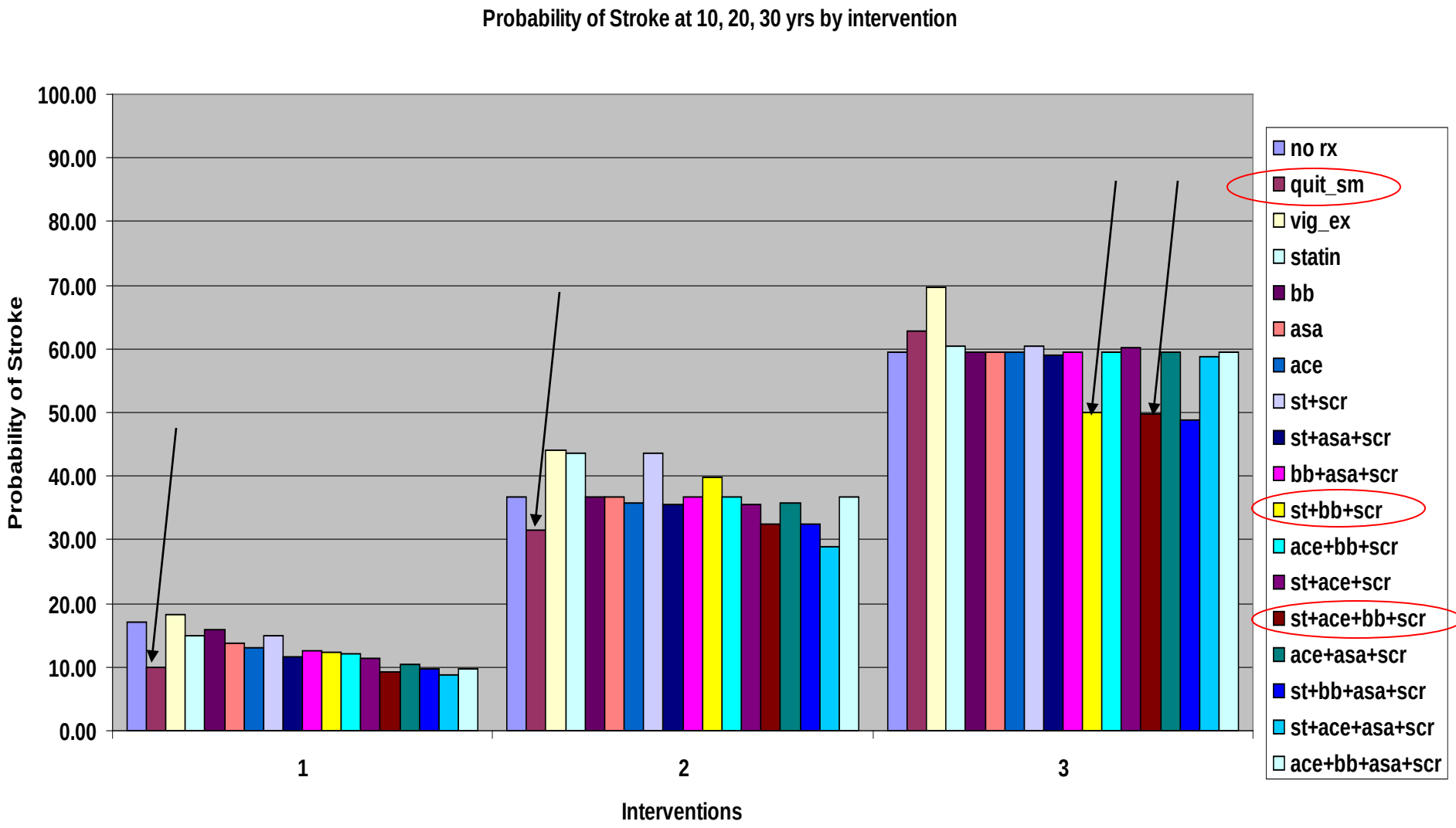
Probability of Stroke at 10, 20, 30 yrs by intervention
Probability of Stroke
100.00
90.00
80.00
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00
1
2
3
Interventions
no rx
quit_sm
vig_ex
statin
bb
asa
ace
st+scr
st+asa+scr
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10-Yr MI ARRs: Comparison of Two Cases

Intervention	50yo WM inactive smoker SBP 160 LDL 130 A1c 9% Baseline Risk 39.1%	70yo BM inactive smoker SBP 160 LDL 130 A1c 9% Baseline Risk 37.9%
Smoking Cessation	19.1%	15.3%
Moderate Exercise	9.4%	16.3%
Aspirin	8.3%	11.5%
SBP to 129	5.1%	9.33%
LDL to 70	0.5%	5.5%
A1c to 7.5	0.2%	3.2%
Beta Blocker	0.7%	4.0%
ACE inhibitor	0.1%	3.7%

Questions?